quinn emanuel trial lawyers | silicon valley
555 Twin Dolphin Drive, 5th Floor, Redwood Shores, California 94065-2139 | TEL (650) 801-5000 FAX (650) 801-5100

WRITER'S DIRECT DIAL NO.
(650) 801-5113

WRITER'S EMAIL ADDRESS
andrewbramhall@quinnemanuel.com

July 25, 2024 **REDACTED FOR PUBLIC FILING**

Re: Case No. 3:21-cv-04062-EMC *Guardant Health Inc. v. Natera, Inc.* re: Sanctions Motion

Dear Judge Chen,

Natera writes in response to Guardant's sanctions reply brief (Dkt. 588) to correct baseless accusations of dishonesty levied against Natera and its attorneys including an allegation that Natera's opposition is part of a "say anything" litigation strategy. As a result of accelerated briefing (Dkt. 579), Natera had less than four days to respond to Guardant's sanctions motion. The subject matter—which includes the failure of Guardant's assay to provide accurate results in the COBRA clinical trial—is also the subject of co-pending *Daubert* motions scheduled to be argued August 29, 2024. Dkt. 575.

Natera's opposition pointed out what it had learned since the parties first addressed COBRA in February 2024: that Guardant was closely involved in many aspects of the trial, had early access to key communications and data, and the NRG oncologists running the study felt misled by Guardant because its assay did not live up to Guardant's representations of 100% performance—mirroring the content of Natera's false advertising claims. In its reply, Guardant refers to this as "a series of new misrepresentations" and "unnecessarily distracting" to rebut (p. 1 and n.2), but goes on to accuse Natera of falsely quoting depositions. These are serious accusations and require a response. As detailed below, Guardant's reply accusations are false.

1. Guardant asserts (n.2, first bullet) that Natera claimed without citation that Guardant's statistical expert referred to COBRA as a "catastrophic failure." But this is the exact language Dr. Heitjan used:
   - "[redacted]" Dkt. 582-30, Ex. 29 (Heitjan July 17, 2024 Tr.) at 158:1-2.

2. Guardant asserts (n.2, second bullet) that it was "false" for Natera to state Dr. Parikh conceded in deposition that Guardant's assay "does not have 100% specificity or PPV but yields 1 in 20 false positives." But this is exactly what Dr. Parikh testified:

- "[redacted]." Ex. A (Parikh July 9, 2024 Tr.) at 51:6-8.
- With respect to specificity, she testified [redacted]." *Id.* at 114:22-24.
- With respect to Reveal's specificity, when asked if 95 percent means about 1 in 20 samples is a false positive, she answered "[redacted]." *Id.* at 38:25-39:8.
- Guardant's Rule 30(b)(6) witness confirmed: "[redacted]" Ex. B (Eagle July 11, 2024 Tr.) at 222:17-23.

3. Guardant takes issue (n.2, third bullet) with Natera's argument that Guardant introduced its new assay design as a result of the COBRA problems. The key issues, however, are that Guardant (a) revised its assay and never disclosed that in this litigation and (b) the revision was to address [redacted]. Indeed, [redacted] Dkt. 582-12, Ex. 11 (GHI00063336) at 1 ([redacted] Guardant ran the COBRA samples [redacted]. *Id.*

4. Guardant asserts (n.2 on page 2, lines 26-28) that Natera made "false" claims and "misrepresentations" [redacted] in the COBRA interim analysis. Natera made no such false claims. [redacted]. Ex. C (NRG-N-000011) at 14 ([redacted]).

At all times, Guardant has had more information about COBRA than Natera. That remains true today. And Guardant has fought tooth and nail to suppress evidence about Reveal's performance in COBRA and keep that evidence from the jury. Indeed, at the outset, on February 15, 2024, when this Court was first considering COBRA's relevance, Guardant's counsel misrepresented that the COBRA trial's closure was "not a reflection on" or "testament to the performance of the assay." Ex. D (2/15/24 Hearing Tr.) at 7:24-8:1. When the Court questioned this statement, and specifically asked whether the trial outcome "suggest[s] the possibility of false positives and false negatives here," Guardant's counsel blamed chemotherapy and answered "***No***." *Id.* at 8:10-14.

Discovery has shown the Court's question was exactly right, and counsel's denial was incorrect. There were false positives in the COBRA trial. Guardant's expert, Dr. Heitjan, confirmed that [redacted]" from the Reveal test was "[redacted]" in the COBRA study population. Ex. E (Heitjan July 17, 2024 Tr.) at 242:20-243:3.

As noted above, COBRA discovery revealed a very important fact: that Guardant changed its assay to address [redacted] problems. This was never voluntarily disclosed by Guardant in this case. The change proves what Natera and Dr. Hochster have said all along—that the Reveal assay by design had significant problems with false positive results and could not filter out CHIP mutations.

Because of the information asymmetry about COBRA, Natera only discovered this critical information by fighting for, and eventually obtaining, COBRA discovery.

The aforementioned discovery, which truly is just the tip of the iceberg, confirms what Natera has contended from the start: that the COBRA trial is highly relevant to key issues in the case. It also shows that, contrary to Guardant's representation to this Court, the study's ultimate failure was directly tied to Reveal's performance, including its propensity for false positives. If anyone deserves any sanctions, it is Guardant, the party that concealed what it knew and now resorts to baseless accusations to try to improve its litigation position.

Respectfully submitted,

QUINN EMANUEL URQUHART & SULLIVAN, LLP

/s/ Andrew J. Bramhall

Andrew J. Bramhall

EXHIBIT A

EXHIBIT FILED
UNDER SEAL

EXHIBIT B

EXHIBIT FILED
UNDER SEAL

EXHIBIT C

EXHIBIT FILED
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EXHIBIT D

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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

Before The Honorable Edward M. Chen

GUARDANT HEALTH, INC., Plaintiff,	)	
VS.	)	**NO. 3:21-cv-4062 EMC**
NATERA, INC., Defendant.	)	

San Francisco, California
Thursday, February 15, 2024

TRANSCRIPT OF PROCEEDINGS BY ZOOM WEBINAR

APPEARANCES BY ZOOM WEBINAR:

For Plaintiffs:

SHEARMAN & STERLING LLP
300 West 6th Street, 22nd Floor
Austin, TX 78701
BY: SAUL H. PERLOFF
ATTORNEY AT LAW

SHEARMAN & STERLING LLP
599 Lexington Avenue
New York, NY 10022
BY: CHRISTOPHER LLOYD LaVIGNE
ATTORNEY AT LAW

KELLER/ANDERLE LLP
18300 Von Karman Ave., Ste. 930
Irvine, CA 92612
BY: JENNIFER LYNN KELLER
CHASE A. SCOLNICK
ATTORNEYS AT LAW

REPORTED REMOTELY BY: Rhonda L. Aquilina, RMR, CRR, CRC
CSR No. 9956, Official U.S. Reporter

APPEARANCES CONT'D.

For Defendant:

QUINN, EMANUEL, URQUHART & SULLIVAN, LLP
555 Twin Dolphin Dr. - 5th Floor
Redwood Shores, California 94065
BY: VICTORIA MAROULIS
BRIAN C. CANNON
MARGARET SHYR
ATTORNEYS AT LAW

QUINN, EMANUEL, URQUHART & SULLIVAN, LLP
865 S. Figueroa Street, 10th Floor
Los Angeles, CA 90017
BY: RYAN SADLER LANDES
ATTORNEY AT LAW

Thursday - February 15, 2024 4:30 p.m.

P R O C E E D I N G S

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THE CLERK: A reminder to everyone observing: These proceedings are being recorded by this court. Any other recording of this proceeding, either by video, audio, including screen shots, or other copying of the hearing is strictly prohibited.

Calling civil action 21-4062, Guardant Health, Inc. versus Natera, Inc.

Counsel, please state your appearances for the record, beginning with the plaintiff.

MR. PERLOFF: Good evening or good afternoon, Your Honor. Saul Perloff on behalf of the plaintiff Guardant Health. With me from my firm is Chris LaVigne. And I'd like to introduce you to our newest team members Jennifer Keller and Chase Scolnick.

MS. KELLER: Good afternoon, Your Honor. Jennifer Keller also on behalf of Guardant.

THE COURT: All right. Thank you. Good afternoon.

MR. SCOLNICK: And good afternoon, Your Honor. Chase Scolnick, also on behalf of Guardant.

THE COURT: All right. Thank you.

MS. MAROULIS: Good afternoon, your Honor. Victoria Maroulis with Quinn, Emanuel for Natera. And with me are my

partners Brian Cannon, Ryan Landes, and Margaret Shyr.

THE COURT: All right. Good afternoon, Ms. Maroulis, and everybody else.

So I thought we should talk as a group here and figure out what we're going to do. It seems to me that this recently I won't say published study, but this revelation of the results of the COBRA trial seemed pretty relevant. I don't know how much weight to be giving it, and there's a lot to be explored, it appears.

But it seems to me that given the nature of this case, I have a hard time seeing how we could just ignore this thing and pretend it didn't happen. And if that's the case, is there a way -- there's obviously some discovery that would need to be done. There's several expert reports. Is it reasonable to expect that all to happen in light of the February 26th pretrial conference and the March 11th start date in this case.

So I want to hear I think first from Guardant. I see what Natera wants to do, and they've got an expert now opining on this. But Guardant's response is that, well, we've got an interview -- or I don't know if you want to depose the authors of the study, file a counter expert report or what.

Maybe I can hear from Guardant what they feel they need to do in order to respond and prepare, assuming this study is going to be admitted or at least discussed at trial.

MR. PERLOFF: Yes, Your Honor. Look, let's take stock

where we are. We are less than four weeks from trial, and having this door open would require us to take significant discovery from, as you suggested, the study sponsor from the principal investigators who did not want the study closed - perhaps from Dr. Parikh whose opinion he -- Dr. Hochster purports. Plus, if you look in his report, he's making comparisons to other data that we would need to take discovery on.

After all of that discovery were taken, we would need to prepare our own rebuttal expert report, do a ***Daubert*** motion probably almost certainly, and we just wouldn't have time to do it. If the Court knows how long it took just to discover the one, you know, Harvard Parikh study that's at issue in this lawsuit.

But I really do want to, if I may, push back on the idea that it's relevant, because certainly the tone and tenor of their argument that this is the most significant thing that has happened might lead one to believe that. But let me attempt to correct the record if I can.

The COBRA study had to do with clearance rates, so in -- specifically you had patients with very low risk of recurrence who -- some of whom were put on chemotherapy and some of who weren't. The Reveal test was used to determine whether or not they had ctDNA. The reason for the closure was because the 16 patients they looked at, they didn't see the clearance rates

that they thought they would on the two arms: The people who got chemo and those that didn't.

If you look at his report, and actually at the data that he shows, it does not have anything to do with sensitivity, specificity, PPV, NPV, pre-surgical sensitivity, lead time, failure rates, turnaround time - none of those things are addressed at all, because that's not what the study was designed to do, and, more importantly, they didn't collect any of the recurrence data.

So to the extent they're trying to make this fit into one of their arguments in the case, for example, that specificity is exaggerated, it can't tell you anything about specificity because nobody knows what happened to these patients.

There are certainly some very interesting questions raised by the study about why, for example, did -- you know, were the blood samples drawn during chemo instead of after; why were the principal investigators ignored, things like that. But those don't have anything to do with the remaining issues in this case.

So especially given where we are, it doesn't seem fair to put Guardant to this Hobson's choice of either getting to finally have its day in court or to properly and fully address this ambush, quite frankly.

And just to put it in context, COBRA is not the only study that has reported data since the close of discovery in this

case 18 months ago. There are other studies that he doesn't address. And of course the whole point of discovery cutoffs is at some point in time you've got to say when. And this Court and the parties said *when* 18 months ago.

And, you know, to constantly refresh or bring up new studies, because there are favorable studies, things that were in his original report that he doesn't address due to new data, we would be -- it would be a never-ending process.

So with due respect, the sound bites from his report and from their papers might lead you to think it has something to do with sensitivity, specificity or the issues that are in this suit, but it doesn't, and that's why the data they actually show you don't say those words, ever.

MR. CANNON: Your Honor, may I respond to that -- or, sorry. Go ahead.

THE COURT: You will, but I'm asking, it may not answer everything, and there may be shortcomings, and there may be some limited, limitations to its relevance. On the other hand, if you're suggesting it's not relevant and not significant, I guess I'm going to hear the other side. But that seems to me a hard position to take here.

MR. PERLOFF: There's no doubt, Your Honor, the decision to close the trial was surprising, especially because the principal investigators argued against it. But, again, it does not -- it is not a reflection on the performance of the

assay. It's not a testament to the performance of the assay. And therein lies the problem, right? Because, again, if the -- this was a determination of whether or not the ctDNA could be used to direct accelerated treatment for patients who ordinarily wouldn't get it. And this analysis that they're focused on was this very limited set of 16 patients, and they received the results and made the decision not to move forward, notwithstanding the recommendation of the principal investigators.

THE COURT: Well, to say it had nothing to do with the performance of the assay, I'm not sure I understand that. I mean, isn't there -- doesn't that suggest the possibility of false positives and false negatives here?

MR. PERLOFF: No. And I want to be clear, it definitely shows that if you draw blood during chemotherapy -- as opposed to the time points that the test is designed for, validated for, and advertised for, which would be after surgery, after chemotherapy -- you're going to get aberrant results, that version of the test.

Because during chemotherapy you have essentially an explosion of dead cells in the bloodstream, right? Because, as I'm sure everybody on this call knows, chemotherapy doesn't just target the cancer cells; it targets all fast-growing cells. And so you have just a ton of circulating DNA, both from cancer and non-cancer.

And without a doubt it showed that if you draw blood during that time period, as opposed to what the study was designed, which was after chemo, you're not going to get the results you think you should get.

But, again, to say that that has anything to do with the advertising that the parties have focused on in this suit, which had to do -- and you know these time points because they've been discussed ***ad nauseam***: Post-surgery, landmark, surveillance. This wasn't testing that, and therein lies the problem, and that's why it's brand new.

THE COURT: All right. Mr. Cannon.

MR. CANNON: Thank you, Your Honor.

So there's quite a bit to unpack there, but I want to address the timing of this first, and that is that the clinical trial was shut down last August, and Guardant has known this. So there's no actual ambush going on here. The clinical trial was shut down and the letters went out to the doctors in August, and Dr. Hochster included that in paragraph 37 of his supplemental report.

And Your Honor is absolutely correct about the relevance. Shutting down a trial like this is a big deal. And the issue is what Your Honor identified, which is the excessive rate of false positives, and that is an issue, as Your Honor knows, that's in the case. It was in Dr. Hochster's original report, and it was the subject of a ***Daubert*** motion. And Your Honor in

CERTIFICATE OF REPORTER

I certify that the foregoing is a correct transcript from the record of proceedings in the above-entitled matter.

Dated: February 16, 2024

Rhonda L. Aquilina, CSR #9956, RMR, CRR, CRC
U.S. Court Reporter

EXHIBIT E

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UNDER SEAL